

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) ~~A~~ An *in vitro* method for generating a mutation in a gene of interest in a hypermutable cell and subsequently stabilizing the genome of the cell comprising the steps of:

growing a hypermutable mammalian cell comprising the gene of interest and a ~~dominant-negative~~ dominant-negative allele of a PMS2 mismatch repair gene under control of an inducible transcriptional regulatory element;

testing the cell to determine whether the gene of interest harbors a mutation; and

restoring mismatch repair activity to the cell by decreasing expression of the ~~dominant-negative~~ dominant-negative allele, thereby generating a mutation in the gene of interest and stabilizing the genome of the cell.

2. (Original) The method of claim 1 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

3. (Original) The method of claim 1 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

4. (Original) The method of claim 1 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

5. (Original) The method of claim 1 wherein the step of testing comprises analyzing the phenotype of the cell.

6. (Currently amended) The method of claim 1 wherein the mammalian cell is made hypermutable by the process of introducing a polynucleotide comprising a ~~dominant-negative~~ dominant-negative allele of a mismatch repair gene into a mammalian cell in vitro, whereby the cell becomes hypermutable.

7. (Currently amended) The method of claim 6 ~~wherein~~ further comprising the step of introducing a reporter gene interrupted with a polymononucleotide tract which causes

a reading frame-shift is introduced into the mammalian cell to permit the monitoring of hypermutability.

8-50. (Withdrawn)